Figure 1. *Astayanax* morphs from surface and cave habitats.

A surface fish (bottom left) and a blind cavefish (bottom right) are shown underneath examples of their respective habitats. Surface habitat (top left) is from Río Tampaón, Mexico and cave habitat (top right) is from Piedras cave, Mexico. Cave habitat photograph courtesy of Jon Jasper; others courtesy of Masato Yoshizawa.

and lateral line enhancement map to the same genomic regions, thereby establishing an association between these traits on a genomic level. In addition, a QTL analysis could reveal potential genomic regions that are unique to each trait, which could highlight factors contributing to vibration attraction behavior that are unrelated to neuromast differences.

The use of genomic approaches also has the potential to provide a more direct test of the concept of nervous system evolution raised earlier: whether sensory evolution alone can drive behavioral change. This idea has previously been difficult to test experimentally. The few studies that have probed this idea have shown that the nervous system can incorporate atypical sensory changes into functional circuits (for example [16]), but that peripheral changes are not sufficient to generate all aspects of an evolutionary shift in brain function [16]. The vibration attraction behavior of cavefish offers another system for addressing this question. Identification of the genomic changes underlying lateral line system elaboration in *Astyanax* could serve as the basis for experiments probing the flexibility of nervous system form and function by manipulating gene function [16–18]. For example, do peripheral changes in neuromast number completely translate into operational circuitry, or are additional downstream changes needed to generate functional behavioral differences? Such an experiment would provide a crucial test of existing concepts, offering invaluable insight into the process of neural circuit evolution.

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Notch Signaling: Filopodia Dynamics Confer Robustness

Though usually thought of as mediating communication between adjacent cells, Notch–Delta signaling can take place over a longer range through cellular processes known as 'filopodia'. A recent study shows how the dynamics of filopodia can confer robustness to Notch–Delta dependent patterning.

Marco Milán[1,2,*] and Stephen M. Cohen[1,*]

Signaling mediated by Notch and Delta is widely used in animals, for instance to pattern the nervous system and muscle progenitors. A classical view of this process stems from the analysis of the *Drosophila* peripheral sensory system and is based on the concept

of the 'equivalence' group, in which a set of cells are all equally capable of becoming the sense organ [1]. Fluctuation in the level of Delta expression allows one cell to gain an advantage and activate Notch in nearby cells. Notch signaling precludes neighboring cells from becoming the sense organ. This process — whereby one cell or group of cells prevents the cells immediately adjacent from adopting the same fate — is called 'lateral inhibition' and is widely used during development to generate patterns of equally spaced structures. Notch and Delta are transmembrane proteins and, as such, their molecular nature is easy to reconcile with a role in mediating such short-range lateral inhibition among adjacent cells. However, in certain contexts, like the *Drosophila melanogaster* compound eye or thorax, Notch-Delta-dependent lateral inhibition helps to single out cells from very large groups of cells, suggesting they may act over several cell diameters. Progress in resolving this apparent inconsistency was made in 2003, when Alexandre and colleagues [2] showed that lateral inhibition was mediated by Delta-containing filopodia that can reach over several cell diameters to activate Notch in distant cells. Baum and colleagues [3] now revisit this process using a combination of live imaging and computational modeling to explore how filopodia are used during lateral inhibition.

The ordered array of small mechanosensory bristles on the *Drosophila* thorax has been one of the classical models for analysis of lateral inhibition (Figure 1), and is the focus of the new study. The precursors of these bristles emerge during pupal development from large pro-neural groups of competent epithelial cells. The emergence of these sensory organ precursor (SOP) cells can be visualized in living animals using a green fluorescent protein (GFP) reporter driven by a gene expressed specifically in differentiating SOP cells. This was combined with a ubiquitously expressed GFP marker to image all epithelial cells, allowing the process of SOP specification and patterning to be followed in real-time through a hole in the pupal case. Two observations emerged. First, the initial SOP pattern is quite sparse within the epithelial sheet, compared to the final pattern. Second, the specification of SOPs is quite dynamic, with some cells being transiently specified and reverting to epithelial identity while other, 'better placed' epithelial cells become SOPs, so as to refine the sparse initial pattern into a well-ordered array of SOPs. This dynamic process of pattern refinement was unexpected. The live imaging approach also lends itself to experimental manipulation by means of laser-assisted cell ablation. The consequences of eliminating an SOP could be followed in real time. As previously shown in other insects and in vertebrates [4,5], ablation of cells that would normally adopt SOP fate induced neighboring cells to turn on SOP-specific gene expression and replace them. Again, the intriguing result lay in the dynamics of the re-patterning process.

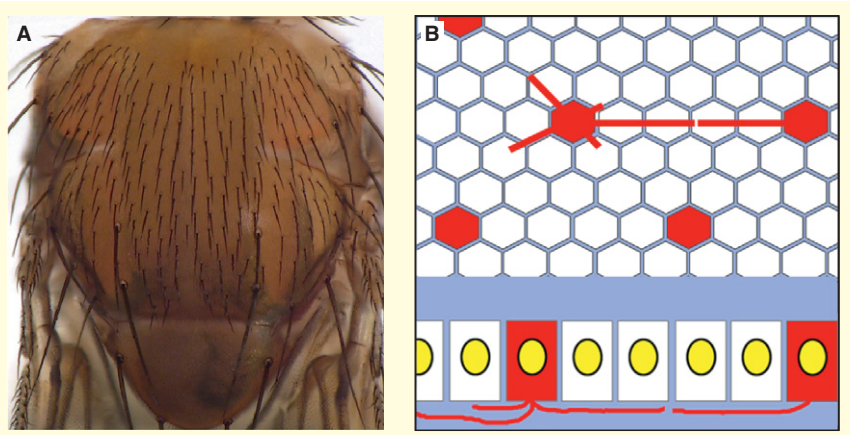

Figure 1. Long-range Notch signaling mediated by dynamic filopodia.

(A) Thorax of an adult fly decorated by an ordered array of small mechanosensory bristles. Note the ordered spacing (image courtesy of Neus Rafel). (B) Cartoon depicting the spatial localization of the sensory organ precursors (SOPs, in red) within the epithelial sheet, which send long basal filopodia to mediate long-range Notch signaling. The upper image shows the epithelial sheet as seen from above, while the lower image shows a side-on view.

The wealth of information available on the dynamics of patterning provided Baum and colleagues [3] with the opportunity to use mathematical modeling to explore mechanisms by which lateral inhibition can generate pattern. The authors began with a model of lateral inhibition based on a previously characterized mathematical framework [6] that uses cell shape and geometry, and assumes short-range cell–cell communication. Not surprisingly, this model produced a pattern of SOPs that was denser than that observed *in vivo*, implying a requirement for long-range cell interactions, as previously suggested [2]. The application of modeling became more interesting, however, when the authors introduced filopodial dynamics as the means of cell–cell signaling (Figure 1B). They found that use of filopodia could explain the transition from the initially sparse to final ordered pattern. Moreover, by testing a broad range of parameters for filopodial length and lifetime, they could predict that the robustness of the patterning process was a function of these two parameters. In the simulation, the final density of the pattern was affected by filopodial length and the speed at which the pattern stabilized was a function of how frequently cells made contact, which is also a function of filopodial lifetime. Too much contact rapidly stabilized an imperfectly ordered pattern, but too little contact did not allow sufficient loss and re-specification of SOPs to refine the pattern.

These predictions allowed Baum and colleagues [3] to put the model to an interesting test. By compromising the activity of the actin regulators SCAR and Rac, they were able to experimentally manipulate the length and stability of filopodia in the epithelium. When the observed experimental parameters were included in the simulation, the model produced a surprisingly accurate prediction of the effects observed in the manipulated animal. The same density of sensory organs was obtained in the computer simulation and in mutants for SCAR or Rac.

Biologists are accustomed to the idea that migrating cells and axons actively sample the environment by sending out filopodia to increase the area that can be sampled for guidance cues [7]. The results of Baum and colleagues [3] add a new twist to the existing notion that epithelial cells use filopodia-like extensions to gather information from cells that are not their immediate neighbors. Long-range cell interactions mediated by these cellular extensions are thought to help receive morphogen signals [8] or collect information about the identity of nearby cells that provide survival cues [9]. The new study [3] highlights the importance of the dynamics of these structures as a part of the information processing system. It is not just extending the range of sampling that is important. The dynamics of sampling can also have a profound impact on how cells use the information that they pick-up from their neighbors to make collective decisions.

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Neurogenetics: Short-Circuiting Sexually Dimorphic Behaviors

It is clear that male and female animals behave differently, but how do those differences arise? New studies show that there are extensive, sex-specific differences in the anatomy of neurons that underlie reproductive behaviors in *Drosophila*.

Michelle Arbeitman* and Ari Winbush

Though behavioral differences between males and females have been a source of fascination and fodder for all manner of entertainment, as well as serious sociological study, there is still meager understanding of how these differences arise in most animal species. These dimorphic behaviors could be determined by the environment, or by biological differences, for example in the structure of neural circuits or in the physiology of architecturally similar neural circuits (Figure 1). Two papers [1,2] in this issue of *Current Biology*, from the Jefferis and Dickson laboratories, report on exciting new progress in understanding how sexually dimorphic behaviors arise in the fruit fly, *Drosophila melanogaster*, by cleverly examining different subsets of neurons known to be important for reproductive behaviors.

Courtship in *Drosophila* is an elaborate ritual performed by males to entice females to mate (reviewed in [3]). These genetically programmed behaviors can be studied in controlled laboratory conditions, and thus are ideally suited for understanding the biological bases of sex-specific behaviors. The courtship ritual consists of a series of sub-behaviors that begins when a male becomes aware of a female and orients towards her. Next, he taps her with his foreleg and receives chemosensory information, after which he will extend a wing and vibrate it to produce a courtship song. If the female does not move away, the male will contact her external genitalia with his proboscis, and if she is receptive, the female will allow the male to copulate with her. After mating, females display post-mating behaviors that include diminished receptivity to male courtship and increased egg laying.

Some of the earliest evidence that *Drosophila* males and females have genetically-specified differences in neural substrates underlying courtship behaviors came from studies examining animals that are mosaic for male and female tissues, as a result of having cells that are either male or female for sex-chromosome composition (reviewed in [3]). These studies showed that several distinct regions of the central nervous system need to be genetically male or female for male or female behaviors to occur, respectively. However, studies examining the anatomy of the adult brain and ventral nerve cord were unable to identify large, overt differences in overall size, or morphology between the male and female nervous system, leaving unanswered what determines these sex-specific behaviors.

Significant progress in understanding the genetic basis of male courtship behavior came from analysis of *fruitless* (*fru*) mutants that display courtship abnormalities. Some *fru* allele combinations result in males that court other males, while other *fru* allele combinations result in males that exhibit reduced courtship, or fail to court at all (reviewed in [4]). In contrast, no phenotypes are observed in *fru* females. The *fru* locus is complex and has at least four